

ACS PRF ANNUAL GRANT REPORT (2018.9-2019.8)

PRF grant number: 57926-DNI-7

Project Title: Stereoselective Polymerization of Petroleum-Derived *O*-Carboxy-anhydride

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AIM 1: Synthesis of new petroleum-derived *O*-carboxyanhydride (OCA) monomer. We have developed a new method to purify OCA monomers in large quantity. Previously, we have to perform repetitive recrystallization to purify OCA monomers. We found out that a quick flash chromatography using pre-dried silica gels and glassware can minimize the workout step and improve the yield. Gram-scale monomers have been prepared within 2 days.

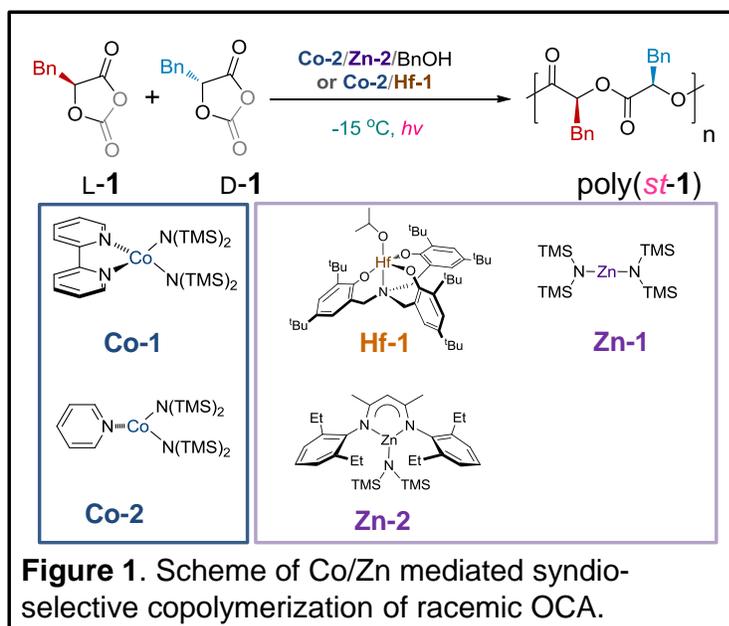
AIM 2: Controlled polymerization of OCA by organometallic catalysts. The PI has worked on developing a new polymer chemistry knowledge base. In work published in 2017 (just before receiving PRF) the PI showed that controlled photoredox polymerization of OCAs produces poly(α -hydroxy acids) (including PLA and PLGA) with various side chain functional groups.¹ This new chemistry, which involves Ni/Ir photoredox catalysis and a Zn-alkoxide for efficient ROP at -15 °C, allows both for rapid synthesis of isotactic polyesters with MWs of >140 kDa and \bar{D} values of <1.1 ($\bar{D} = M_w/M_n$; M_n , number-average MW; M_w , weight-average MW). Notably, even for high-MW poly(L-1) ($M_n = 140.5$ kDa), no epimerization of the α -methine hydrogen is observed in the homodecoupling ¹H NMR spectrum.¹ The polymerization is first order with respect to L-1, suggesting the living nature of the photoredox ROP.¹

This recent development of Ni/Zn/Ir mediated OCA polymerization led us to wonder whether other transition metal complexes, such as the Co complexes used in *N*-carboxyanhydride polymerization, could be applied to our protocol. This did indeed prove to be the case, with an unexpected twist: specifically, Co(HMDS)₂ (HMDS = hexamethyldisilazane) could replace both the Ni catalyst and the Ir photocatalyst and mediated ROP of OCA L-1 at room temperature in the presence of Zn-1 and benzyl alcohol ([L-1]/[Co(HMDS)₂]/[Zn-1]/[BnOH] = 500/1/1/1) and light from a blue LED (300–500 nm) to afford poly(L-1) ($M_n = 65.0$ kDa and $\bar{D} = 1.06$). This fortuitous discovery led us to hypothesize that the Co complex not only oxidatively inserted into the OCA but also functioned as a photocatalyst for decarboxylation. We then evaluated the activities of various Co complexes in Co/Zn-mediated photoredox ROP of L-1 ([Co] = [Zn-1] = [BnOH]). We noticed that Co^I and Co^{III} and most Co^{II} complexes were much less effective than Co(HMDS)₂. The addition of ligands to Co(HMDS)₂ greatly improved M_n values and monomer conversions. When the [1]/[Zn-1] ratio was elevated to 700/1, Co complexes with ligands based on bpy and phenanthroline led to controlled photoredox ROP with M_n values close to the calculated molecular weight (MW_{cal}) of 103.7 kDa). When the [1]/[Zn-1] ratio was increased to 800/1, polymerization at room temperature generally afforded polymers with M_n values that were lower than the MW_{cal} values; whereas the increased M_n s and narrow \bar{D} s were achieved when the reaction temperature was decreased to 0 °C. At such a high [1]/[Zn-1] ratio (800/1), Co-1 (i.e., (bpy)Co(HMDS)₂) outperformed other complexes, affording a polymer with a M_n of 114.0 kDa, which is close to the MW_{cal} (118.5 kDa), and a narrow \bar{D} of 1.03.

However, when the initial [L-1]/[Co-1]/[Zn-1] ratio was 900/1/1, monomer conversion was only 43.7% at 0 °C, indicating the occurrence of side reactions. When the reaction temperature was decreased to -15 °C, the M_n values of the poly(L-1) products increased linearly with initial [L-1]/[Co-1]/[Zn] ratio up to 1100/1/1 and were slightly higher than the MW_{cal} values, with the \bar{D} values of all of the obtained polymers <1.1. No epimerization of the α -methine hydrogen was observed in the homodecoupled ¹H NMR spectra of the polymers, including high-molecular-weight poly(L-1) ($M_n = 215.2$ kDa), suggesting that the Co complex did not affect the chirality of L-1 during the ROP. Moreover, electrospray ionization mass spectrometry analysis of oligo(L-1) at a [L-1]/[Zn] ratio of 5/1 confirmed attachment of the BnO- group to the oligomer, suggesting that a Zn-alkoxide was involved in ring-opening and chain propagation.

By means of a series of control experiments, we demonstrated that each of the catalytic components was necessary. At an initial [L-1]/[Co-1]/[Zn] ratio of 700/1/1, neither Co-1 nor Zn-1, either alone or in the presence of BnOH, efficiently initiated the polymerization. Additionally, monomer conversion was incomplete in the absence of BnOH or light. When the LED was replaced by sunlight, the reaction still proceeded smoothly to completion within 1 h at 0 °C. We then examined the kinetics of photoredox ROP of L-1 at -15 °C by varying the concentration of each reaction component. The reaction was first-order with respect to L-1, whereas the reaction orders with respect to Co-1, Zn-1 and BnOH were 2.33 ± 0.20 , 2.64 ± 0.03 , and 0 respectively. These results indicate that the rate of chain propagation was independent of BnOH concentration.

With a set of optimized conditions in hand, we explored the generality of the Co/Zn-mediated photoredox polymerization by carrying out reactions of other OCAs (L-2, L-3, and L-4, at room temperature; L-5 at -15 °C). In all instances, polymerization proceeded smoothly, as was the case for the formation of poly(L-1); the M_n values of



stereocomplex counterparts. Furthermore, in one-pot photoredox copolymerization of two different OCAs, the use of such Zn complex mediates kinetic resolution of the co-monomers during enchainment and shows a chirality preference that allows for the synthesis of gradient copolymers.

To synthesize syndioselective OCA monomers, one way is to tune catalyst ligands as proposed in the PRF proposal. However, we found it is difficult to find an optimal catalyst (including Zn, Hf, Y etc.) for the syndioselective OCA polymerization to generate high molecular weight polymers. We then explored whether our Co/Zn catalytic system could be adapted for syndioselective ROP of OCAs. We began by carrying out photoredox ROP reactions of racemic OCAs using **Co-1** or **Co-2** and **Zn-2**, which reportedly afford syndiotactic poly(lactic acid) from *meso*-lactide. We found that the ligand of the Co complex markedly affected the polymerization kinetics. Specifically, **Co-2**, a Co^{II} complex with a less bulky pyridine ligand than that of **Co-1**, initiated controlled polymerization of *rac-1* under the optimized photoredox conditions at $-15\text{ }^{\circ}\text{C}$ ($[\text{L-1}]/[\text{D-1}]/[\text{Co-2}]/[\text{Zn-2}]/[\text{BnOH}] = 100/100/1/1/1$) and afforded syndiotactic copolymer poly(*st-1*) with a P_r (probability of racemic dyad formation) of 0.88 ($M_n = 57.7\text{ kDa}$, $\bar{D} = 1.14$). Note that when **Zn-2** was replaced with **Zn-1**, polymerization was not efficiently initiated; when **Co-2** was replaced by **Co-1**, the obtained polymer had a large \bar{D} of 1.28; **Zn-2** alone was incapable to initiate polymerization of *rac-1*. Additionally, we found that the combination of **Co-2** with **Hf-1**, a reported syndioselective Hf-alkoxide complex for *rac*-lactide and *rac-4* polymerization, provided syndiotactic copolymers when used for the photoredox ROP of *rac-1* with a P_r of 0.89 ($[\text{L-1}]/[\text{D-1}]/[\text{Co-2}]/[\text{Hf-1}] = 200/200/1/1$; $M_n = 96.6\text{ kDa}$, $\bar{D} = 1.06$; Table 3, entry 8; Supplementary Fig. 40e). Changing the $[\text{L-1}]/[\text{D-1}]$ ratio from 1/1 to 2/1 or 1/2 markedly decreased the P_r value from 0.89 to 0.77 ($[\text{Co-2}]/[\text{Hf-1}] = 1/1$), confirming our assigned tetrad peaks. Therefore, it looks promising to further develop Co/Zn and Co/Hf system with chiral Zn or Hf ligands for syndioselective ROP of OCAs (Figure 1).

IMPACT. This PRF grant substantially supports my research in the living polymerization of *O*-carboxyanhydrides. During the first year, we have published the Nature Communications paper based on our research progress (reference # 2). The PI truly appreciates the support from this grant to help the start of his early career. During the first year, three graduate students were supported by this grant. They also traveled to the ACS national conference to present the research.

REFERENCE

- (1) Feng, Q.; Tong, R. Controlled Photoredox Ring-Opening Polymerization of *O*-Carboxyanhydrides. *J. Am. Chem. Soc.* **2017**, *139*, 6177-6182.
- (2) Feng, Q.; Yang, L.; Zhong, Y.; Guo, D.; Liu, G.; Xie, L.; Huang, W.; Tong, R. Stereoselective photoredox ring-opening polymerization of *O*-carboxyanhydrides. *Nat. Commun.* **2018**, *9*, 1559.

the obtained polymers were close to the MW_{cal} values, the \bar{D} values were <1.2 , and the α -methine hydrogens did not epimerize. Note that considerable epimerization of **L-5**, which has an acidic α -methine proton, is often observed during ROP, but this was not so in our system. Moreover, diblock copolymers and a triblock copolymer could be readily prepared in one pot by sequential addition of the monomers, and excellent control of the M_n and \bar{D} values was achieved.

AIM 3: Stereoselective ROP of OCA. In 2018 (see previous report), the PI developed a new chemistry that allows for stereoselective ROP of OCAs using Ni/Zn/Ir catalytic system.² The obtained stereoblock copolymers are highly isotactic with high molecular weights ($>70\text{ kDa}$) and narrow molecular weight distributions ($M_w/M_n < 1.1$), and they display distinct melting temperatures that are similar to their